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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,370	02/21/2001	Etsuro Ogata	OGATA4	9907
1444	7590	02/25/2005	EXAMINER	
BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			HARRIS, ALANA M	
		ART UNIT	PAPER NUMBER	
		1642		

DATE MAILED: 02/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/763,370	OGATA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 19 November 2004.  
 2a) This action is **FINAL**.                            2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 2-6,8-17,20 and 21 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 2-6, 8-17, 20 and 21 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) Notice of References Cited (PTO-892)                            4) Interview Summary (PTO-413)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)                            Paper No(s)/Mail Date. \_\_\_\_\_.  
 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_                            5) Notice of Informal Patent Application (PTO-152)  
 \_\_\_\_\_                            6) Other: \_\_\_\_\_.

**DETAILED ACTION**

***Response to Amendments and Arguments***

1. Claims 2-6, 8-17, 20 and 21 are pending.

Claims 6, 8-11, 16, 17, 20 and 21 have been amended.

Claims 19 and 22-24 have been cancelled.

Claims 2-6, 8-17, 20 and 21 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Withdrawn Rejections***

***Claim Rejections - 35 USC § 112***

3. The rejection of claims 2-6, 8-17, 20 and 21 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing metastasis of malignant tumor to bone using osteocalcin and bone alkaline phosphatase (BALP), does not reasonably provide enablement for diagnosing metastasis of malignant tumor to bone using any other osteoclast or osteoblast marker, nor a method of evaluating the therapeutic efficacy of a drug using a marker that reflects osteoblast and osteoclast activity is withdrawn in light of Applicants' arguments. Claims 19 and 22-24 have been cancelled.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2-6, 8-15, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants have amended claim 6 to include the recitation,

"...using markers that reflect the activity of osteoblasts and markers that reflect the action of osteoclasts,

1) wherein the markers...are

- a) one or more markers..., and
- b) one or more markers...,

2) wherein the one or more markers... bone metastasis are diagnosed by monitoring said markers." Likewise, claim 8 has been amended in the same manner.

In essence Applicants have amended the claims to broaden the scope. As the claims currently read the methods now depend on the implementation of a multitude of markers. Applicants have not pointedly expressed wherein the specification support can be found for these limitations that now read on a method using an arbitrary number

of markers. Applicants should delete the new matter or pointedly express where in the specification by page and line number where support can be found for these new limitations.

5. The rejection of claims 2-6, 8-17, 20 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained and made. Claims 19 and 22-24 have been cancelled.

a. Claims 2-6, 20 and 21 are vague and indefinite because it is not clear if the first marker or second marker is A or B and the method steps are not clear. Applicants ardently argue that the present invention is not all that complex and that the claims are directed to those persons skilled in the present art. Applicants also provide a number of cosmetic amendments. These points of view and arguments have been considered, but found unpersuasive.

Applicants do not address the rejections specifically in a manner that aids in one of ordinary skill in the art to have a clear understanding of the method. Furthermore, Applicants have added the recitation "...the ratio of A/B is a Z value of an A to Z value of B...". This recitation is indefinite. As stated previously in the Action mailed July 15, 2003 independent claim 6 sets forth two markers, the first reflects osteoblast activity, wherein the second reflects osteoclast activity. However, dependent claim 20 only lists markers associated solely with osteoblast activity. Likewise, dependent claim 21 sets

forth, A is an osteoclast marker and B lists both osteoblast and osteoclast markers.

Applicants are requested to discriminately review all claims and ensure clarity.

b. The arguments presented in section a read on the instant rejection and they are found unpersuasive. Claims 8-17 and 23 are vague and indefinite because it is not clear from the claims how the two markers are used in ascertaining efficacy of a drug and the method steps are not clear. While it notes that one marker represents osteoclast activity and the other is for osteoblast activity how is these values are to be used is not expressed in the claims. Furthermore, dependent claim 17 presents a ratio wherein A is a osteoclast marker. The list for what is B comprises both osteoblasts and osteoclast markers. Applicants are requested to discriminately review all claims and ensure clarity. Applicants have added the recitation "...the ratio of A/B is a Z value of an A to Z value of B...". This recitation is indefinite.

c. The recitation "the marker" in claims 12-15, line 2 lacks proper antecedent bases in independent claim 8.

#### ***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 2-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Koizumi et al. (J. Cancer Res. Clin. Oncol. 121: 542-548, 1995). Koizumi discloses a method of

measuring osteoclastic (pyridinoline-cross-linked carboxyterminal telopeptide, ICTP and deoxypyridinoline, Dpd) and osteoblastic markers (procollagen I carboxyterminal peptide, PICP, bone gla protein, BGP and alkaline phosphatase) in order to diagnose and detect bone metastasis in patients with breast, prostate and lung cancer, see Abstract; page 543, Table 1 and corresponding text; page 544, Table 2 and Figures 1a-e and corresponding text; page 545, Figures 2a-e and Table 3 and corresponding text; page 546, Figures 3a-e and corresponding text. "The levels of markers tended to rise as the grade of metastasis increased." The values of various bone metabolic markers in all the cancers seemed to be a function of the grade of bone metastasis and bone metastatic burden, see page 543, column 2, second paragraph; bridging paragraph of pages 545 and 546; and page 546, column 1, first full paragraph.

9. Claims 8-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Martinetti et al. Tumor Biol. 18: 197-205, 1997). Martinetti discloses a method of evaluating osteoclastic and osteoclastic markers with bone metastases and treated with formestane, see abstract. The osteoclastic marker measured was ICTP (a bone resportion marker) and the osteoblastic markers measured were PICP (a proliferation marker), osteocalcin or BGP (a mineralization marker) and BALP (a matrix formation marker), see abstract and Table 2 on page 200 and corresponding text; Table 3 on page 201 and corresponding text. Four of these markers were assayed and evaluated to determine the biological efficacy of the aromatase inhibitor formestane, see bridging sentence of columns 1 and 2 of page 198.

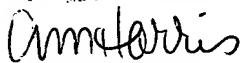
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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm, with alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**ALANA M. HARRIS, PH.D.  
PRIMARY EXAMINER**



Alana M. Harris, Ph.D.  
22 February 2005